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IgA Nephropathy

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The Biological Effects of Secretory IgA on Human Mesangial Cells

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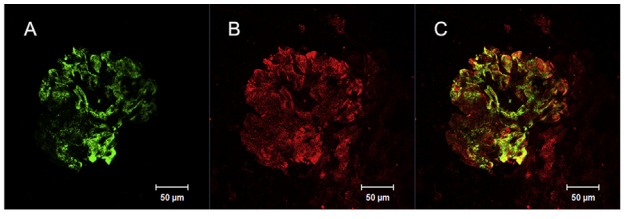
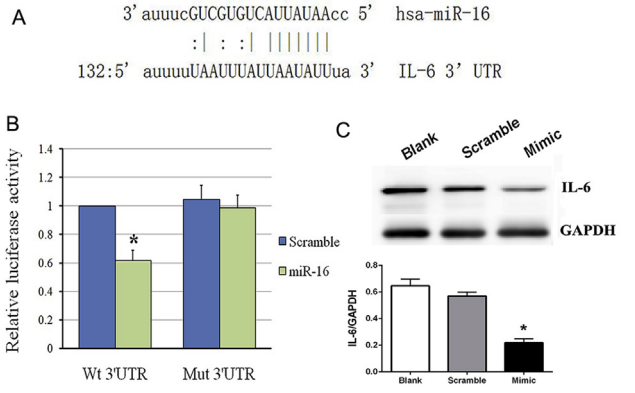
Objectives: IgA nephropathy (IgAN) is the most common form of primary glomerulonephritis, and often aggravates by mucosal infection. Secretory IgA (SIgA) is the dominant immunoglobulin in mucosal immunity, and is deposited in the mesangium in IgAN. The biological effects of SIgA on mesangial cells are poorly understood, and the mechanism is still not clear.
Methods: SIgA was purified from the saliva of IgAN patients with glomerular SIgA deposition (P-SIgA). And polymeric IgA (pIgA) was isolated from the serum of IgAN patients without its deposition (P-pIgA). In addition, the saliva and serum of healthy volunteers were collected to purify SIgA and pIgA as controls (N-SIgA and N-pIgA). The biological effects of SIgA and pIgA on human mesangial cells (HMCs) were compared. We also studied the molecular mechanism of microRNA regulating the inflammatory effects of SIgA on HMCs using dual-luciferase assay.
Results: Fifty-five of 176 patients had SIgA deposition in glomerular (Figure 1). P-SIgA stimulated HMCs at a higher ratio of proliferation compared with N-SIgA ($P < 0.05$). P-SIgA stimulated HMCs to release more interleukin (IL)-6, IL-8, monocyte chemotactic protein 1, transforming growth factor-β1 and fibronectin at protein synthesis (by 2-, 1.6-, 1.9-, 1.3- and 1.5-fold, respectively) and mRNA expression (by 2.3-, 1.4-, 2.1-, 2.4- and 1.5- fold, respectively), when compared with N-SIgA ($P < 0.05$ for all). The proliferation and productions of IL-6, IL-8, fibronectin in mesangial cells stimulated by P-SIgA were significantly lower than that stimulated by P-pIgA ($P < 0.05$ for all). miR-16 targeted the 3'-untranslated region of IL-6 and suppressed its translation in mesangial cells induced by SIgA (Figure 2).



These were detected in frozen sections of a patient with IgA nephropathy (magnification × 200). Bar = 50 μm. A. Mesangial deposition of IgA (green). B. Deposition of secretory component (red). C. Merging of IgA and secretory component (yellow).

Figure 1 Colocalization of secretory component and IgA detected by immunofluorescence.



A. The putative miR-16 binding sequences for the IL-6 3' UTR. B. Dual-luciferase reporter co-transfection with miR-16 and wild-type or mutant 3' UTRs of IL-6. The reporter containing the wild-type 3' UTR significantly suppressed luciferase activity. *P<0.001 compared with the control group. C. Human mesangial cells (HMCs) were transfected with mimic miR-16 and induced with SIgA purified from IgAN patients. Over-regulation of miR-16 inhibited expression of IL-6 at the post-transcriptional level. Protein level of IL-6 in supernatant of HMCs detected by Western blot in three groups; GAPDH as a reference. *P<0.001 compared with the control group. Blank: nontransfected blank group; Scramble: transfected with scrambled miR-16; Mimic: transfected with miR-16 mimic.

Figure 2 IL-6 was identified as a target of miR-16 in human mesangial cells.

Conclusion: The biological effects of SIgA on mesangial cells differ from those of pIgA. SIgA stimulates mesangial cell proliferation and production of proinflammatory cytokines. IL-6 production is regulated by miR-16 in mesangial cells.

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Xuanfeibushen Decoction Alleviates Kidney Damage by Regulating Th17/Treg Cells in α-HS Infected IgA Nephropathy Mice

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Objective: The syndrome of asthenia in origin and sthenia in superficiality is considered as the important mechanism of IgA nephropathy (IgAN) in Traditional Chinese Medicine, and Xuanfeibushen Decoction (XD) is used in treating IgAN. The Th17/Treg imbalance plays an important role in IgAN, but it is